PATENT
Attorney Docket No. 207596
DHHS Ref: E-200-98/3

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#7 Amdt. A/ Elec. Examiner 1/14/03

In re Application of:

Erickson et al.

Application No. 09/720,276

Group Art Unit: 1648

Examiner: S. A. Foley

Filed: March 7, 2001

For: FITNESS ASSAY AND ASSOCIATED METHODS

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

Commissioner for Patents
Washington, D.C. 20231

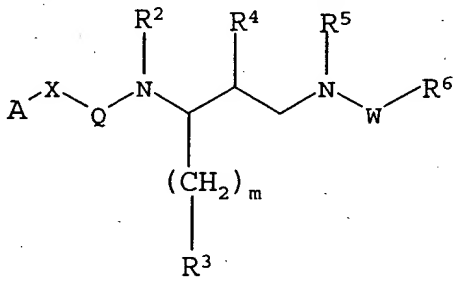
Dear Sir:

In response to the Office Action dated October 2, 2002, please enter the following amendments and consider the following remarks.

AMENDMENTS

Please replace claims 47 and 64-66 with the following:

47. (Amended) A method of preventing the development of drug resistance in an HIV-infected mammal, said method comprising administering to said HIV-infected mammal a drug resistance-inhibiting effective amount of a compound of the formula:

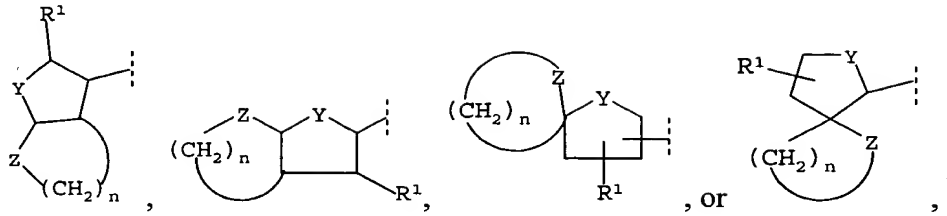


(I),

or a pharmaceutically acceptable salt, a prodrug, or an ester thereof, or a pharmaceutically acceptable composition of said compound, said salt, said prodrug, or said ester thereof, wherein:

A is a group of the formula:

A cont'd.



R^1 is H or an alkyl, an alkenyl, an alkynyl, a cycloalkyl, a cycloalkylalkyl, an aryl, an aralkyl, a heterocycloalkyl, a heterocycloalkylalkyl, a heteroaryl, or a heteroaralkyl, in which at least one hydrogen atom is optionally substituted with a substituent selected from the group consisting of OR^7, SR^7, CN, NO_2, N_3, and a halogen, wherein R^7 is H, an unsubstituted alkyl, an unsubstituted alkenyl, or an unsubstituted alkynyl;

Y and Z are the same or different and [are independently] each is selected from the group consisting of CH_2, O, S, SO, SO_2, NR^8, $R^8C(O)N$, $R^8C(S)N$, $R^8OC(O)N$, $R^8OC(S)N$, $R^8SC(O)N$, $R^8R^9NC(O)N$, and $R^8R^9NC(S)N$, wherein R^8 and R^9 are each selected from the group consisting of H, an unsubstituted alkyl, an unsubstituted alkenyl, and an unsubstituted alkynyl;

A1 cont'd.

n is an integer from 1 to 5;

X is a covalent bond, CHR^{10}, $CHR^{10}CH_2$, CH_2CHR^{10}, O, NR^{10}, or S, wherein R^{10} is H, an unsubstituted alkyl, an unsubstituted alkenyl, or an unsubstituted alkynyl;

Q is C(O), C(S), or SO_2;

R^2 is H, a C_1-C_6 alkyl, a C_2-C_6 alkenyl, or a C_2-C_6 alkynyl;

m is an integer from 0 to 6;

R^3 is a cycloalkyl, a heterocycloalkyl, an aryl, or a heteroaryl in which at least one hydrogen atom is optionally substituted with a substituent selected from the group consisting of alkyl, $(CH_2)_pR^{11}$, OR^{12}, SR^{12}, CN, N_3, NO_2, $NR^{12}R^{13}$, $C(O)R^{12}$, $C(S)R^{12}$, CO_2R^{12}, $C(O)SR^{12}$, $C(O)NR^{12}R^{13}$, $C(S)NR^{12}R^{13}$, $NR^{12}C(O)R^{13}$, $NR^{12}C(S)R^{13}$, $NR^{12}CO_2R^{13}$, $NR^{12}C(O)SR^{13}$, and a halogen, wherein:

p is an integer from 0 to 5;

R^{11} is a cycloalkyl, a heterocycloalkyl, an aryl, or a heteroaryl in which at least one hydrogen atom is optionally substituted with a substituent selected from the group consisting of a halogen, OH, OCH_3, NH_2, NO_2, SH, and CN; and

R^{12} and R^{13} are the same or different and each is selected from the group consisting of H, an unsubstituted alkyl, an unsubstituted alkenyl, and an unsubstituted alkynyl;

R^4 is OH, =O (keto) or NH_2, wherein, when R^4 is OH, it is optionally in the form of a pharmaceutically acceptable ester or prodrug, and when R^4 is NH_2, it is optionally an amide,

a hydroxylamino, a carbamate, a urea, an alkylamino, a dialkylamino, a protic salt thereof, or a tetraalkylammonium salt thereof;

R^5 is H, a C_1-C_6 alkyl radical, a C_2-C_6 alkenyl radical, or $(CH_2)_qR^{14}$, wherein q is an integer form 0 to 5, and R^{14} is a cycloalkyl, a heterocycloalkyl, an aryl, or a heteroaryl radical in which at least one hydrogen atom is optionally substituted with a substituent selected from the group consisting of a halogen, OH, OCH_3, NH_2, NO_2, SH, and CN;

W is C(O), C(S), or SO_2; and

R^6 is a cycloalkyl, heterocycloalkyl, aryl, or heteroaryl radical in which at least one hydrogen atom is optionally substituted with a substituent selected from the group consisting of a halogen, OR^{15}, SR^{15}, $S(O)R^{15}$, SO_2R^{15}, $SO_2NR^{15}R^{16}$, $SO_2N(OH)R^{15}$, CN, $CR^{15}=NR^{16}$, $CR^{15}=N(OR^{16})$, N_3, NO_2, $NR^{15}R^{16}$, $N(OH)R^{15}$, $C(O)R^{15}$, $C(S)R^{15}$, CO_2R^{15}, $C(O)SR^{15}$, $C(O)NR^{15}R^{16}$, $C(S)NR^{15}R^{16}$, $C(O)N(OH)R^{15}$, $C(S)N(OH)R^{15}$, $NR^{15}C(O)R^{16}$, $NR^{15}C(S)R^{16}$, $N(OH)C(O)R^{15}$, $N(OH)C(S)R^{15}$, $NR^{15}CO_2R^{16}$, $N(OH)CO_2R^{15}$, $NR^{15}C(O)SR^{16}$, $NR^{15}C(O)NR^{16}R^{17}$, $NR^{15}C(S)NR^{16}R^{17}$, $N(OH)C(O)NR^{15}R^{16}$, $N(OH)C(S)NR^{15}R^{16}$, $NR^{15}C(O)N(OH)R^{16}$, $NR^{15}C(S)N(OH)R^{16}$, $NR^{15}SO_2R^{16}$, $NHSO_2NR^{15}R^{16}$, $NR^{15}SO_2NHR^{16}$, $P(O)(OR^{15})(OR^{16})$, an alkyl, an alkoxy, an alkylthio, an alkylamino, a cycloalkyl, a cycloalkylalkyl, a heterocycloalkyl, a heterocycloalkylalkyl, an aryl, an aryloxy, an arylamino, an arylthio, an aralkyl, an aryloxyalkyl, an arylaminoalkyl, an aralkoxy, an (aryloxy)alkoxy, an (arylamino)alkoxy, an (arylthio)alkoxy, an aralkylamino, an (aryloxy)alkylamino, an (arylamino)alkylamino, an (arylthio)alkylamino, an aralkylthio, an (aryloxy)alkylthio, an (arylamino)alkylthio, an (arylthio)alkylthio, a heteroaryl, a heteroaryloxy, a heteroarylamino, a heteroarylthio, a heteroaralkyl, a heteroaralkoxy, a heteroaralkylamino, and a heteroaralkylthio,

wherein R^{15}, R^{16}, and R^{17} are the same or different and each is H, an unsubstituted alkyl, or an unsubstituted alkenyl,

wherein, when at least one hydrogen atom of R^6 is substituted with a substituent other than a halogen, OR^{15}, SR^{15}, CN, N_3, NO_2, $NR^{15}R^{16}$, $C(O)R^{15}$, $C(S)R^{15}$, CO_2R^{15}, $C(O)SR^{15}$, $C(O)NR^{15}R^{16}$, $C(S)NR^{15}R^{16}$, $NR^{15}C(O)R^{16}$, $NR^{15}C(S)R^{16}$, $NR^{15}CO_2R^{16}$, $NR^{15}C(O)SR^{16}$, $NR^{15}C(O)NR^{16}R^{17}$, or $NR^{15}C(S)NR^{16}R^{17}$, at least one hydrogen atom on said substituent is optionally substituted with a halogen, OR^{15}, SR^{15}, CN, N_3, NO_2, $NR^{15}R^{16}$, $C(O)R^{15}$, $C(S)R^{15}$, CO_2R^{15}, $C(O)SR^{15}$, $C(O)NR^{15}R^{16}$, $C(S)NR^{15}R^{16}$, $NR^{15}C(O)R^{15}$, $NR^{15}C(S)R^{16}$, $NR^{15}CO_2R^{16}$, $NR^{15}C(O)SR^{16}$, $NR^{15}C(O)NR^{16}R^{17}$, or $NR^{15}C(S)NR^{16}R^{17}$; and

wherein a mutant virus that is capable of evolving from the HIV virus infecting said mammal has lower fitness, relative to said HIV virus infecting said mammal, in the presence of said compound.